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Patent Number

Inventor: Peter Ramm et al.

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TRANSMITTAL OF APPEAL BRIEF	Docket No. 01191/100E235-US2

In re Application of: Peter Ramm et al.

Application No.	Filing Date	Examiner	Group Art Unit
09/915,813-Conf. #9938	July 25, 2001	J. S. Brusca	1631

Invention: PROCESS FOR EVALUATING CHEMICAL AND BIOLOGICAL ASSAYS

TO THE COMMISSIONER OF PATENTS:

Transmitted herewith is the Appeal Brief in this application, with respect to the Notice of Appeal filed: November 19, 2004.

The fee for filing this Appeal Brief is $500.00.

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Docket No.: 01191/100E235-US2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Peter Ramm et al.

Application No.: 09/915,813 Confirmation No.: 9938

Filed: July 25, 2001 Art Unit: 1631

For: PROCESS FOR EVALUATING CHEMICAL AND BIOLOGICAL ASSAYS Examiner: J. S. Brusca

APPELLANTS' BRIEF ON APPEAL UNDER 37 C.F.R. § 1.192

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is Appellant's brief under 37 C.F.R. §1.192 for the appeal of the final Office Action mailed May 19, 2004 by Examiner John S. Brusca in the above-identified patent application.

As required under § 41.37(a), this brief is filed within two months of the November 19, 2004 Notice of Appeal filed in this case, and is in furtherance of said Notice of Appeal.

This brief contains items under the following headings as required by 37 C.F.R § 41.37 and M.P.E.P. § 1206:

I.	Real Party In Interest
II	Related Appeals and Interferences
III.	Status of Claims
IV.	Status of Amendments
V.	Summary of Claimed Subject Matter

I. REAL PARTY IN INTEREST

The real party in interest for this appeal is:

GE Healthcare.

Rights in and to this application have been assigned to this party.

II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS

There are no other appeals, interferences, or judicial proceedings which wi l directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

There are 7 claims pending in application, i.e. claims 5-7, 11, 14, 16 and 17. They are reproduced in **Appendix A**.

B. Current Status of Claims

1. Claims canceled: 1-4, 8-10, 12-13, 15

2. Claims withdrawn from consideration but not canceled: none

3. Claims pending: 5-7, 11, 14, 16, and 17

4. Claims allowed: none

5. Claims rejected: 5-7, 11, 14, 16, and 17

Claims 5-7, 11, 14, 16 and 17 stand rejected under 35 U.S.C. §102(a) as being anticipated by *Ratio-Based Decisions and the Quantitative Analysis of cDNA Microarray Images*, Journal of Biomedical Optics, Vol. 2 No. 4, pages 364-374 (October 1997), Chen et al. ("Chen").

C. Claims On Appeal

The claims on appeal are claims 5-7, 11, 14, 16, and 17.

For the purpose of the present appeal, Appellants request that the claims be considered to form a single group.

IV. STATUS OF AMENDMENTS

In response to the final Office Action mailed May 19, 2004, Appellants filed a Request for Reconsideration on October 22, 2004. The Examiner responded thereto in an Advisory Action mailed November 4, 2004. In the Advisory Action, the Examiner indicated that the Request for Reconsideration did not place the application in condition for allowance.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Hybridization arrays containing a large number of specimens are measured photographically, usually with an electronic camera. The goal is to distinguish different response classes, such as the presence or absence of a signal. The light signals that are measured are

relatively dim and are accompanied by spurious light. The process of discriminating among response classes is therefore a statistical one involving a probability distribution which could be thought of as a graph of specimen light intensity or frequency versus the probability that the response class achieves that intensity (see e.g. Fig. 1). Different distributions may overlap.

According to the claimed subject matter, discrimination of probe response classes within arrays is possible. Element measurements within arrays may reflect different classes of values, e.g., signals, non-signal background, a family of genes associated with disease states, etc. (Specification, Rectified Sheet No. 8, lines 30-37.) The claimed subject matter "uses a mathematically derived approach for deconvolving any mixture of distinct underlying distributions." (Specification, Rectified Sheet No. 8, line 38 through Sheet No. 9, line 2.) Specifically, the claimed subject matter is a method of treating overlapping distributions within the arrayed data by modeling dual or multiple distributions. A mathematical mixture model is applied to deconvolve distributions and regions of overlap between distributions. (Specification, Rectified Sheet No. 9, lines 4-10.)

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether the Examiner erred in holding that claims 5-7, 11, 14, 16 and 17 are unpatentable under 35 U.S.C. §102(a) as anticipated by Chen.

VII. ARGUMENT

The Chen article does not disclose deconvolving overlapping portions of distributions. Therefore, Chen does not disclose each and every feature of the invention of claims 5-7, 11, 14, 16 and 17. Thus, Chen does not anticipate the claimed invention.

This Appeal Brief is being filed in response to the Official Action mailed on May 19, 2004. Claims 5-7, 11, 14, 16 and 17 are pending in this application. The Examiner contends that claims 5-7, 11, 14, 16 and 17 are unpatentable under 35 U.S.C. §102(a) as being anticipated by Chen.

In traversing this rejection, Appellants noted that:

> [I]n accordance with the claims, the present invention involves deriving *distributions* of data obtained from physical measurements and deconvolving overlapping portions of such *distributions*. There is not the slightest suggestion in Chen that any derived data *distributions* might overlap, that deconvolving overlapping portions should be performed, or that it would be of any benefit. Accordingly, Chen does not teach or suggest primary features of the present invention and could not anticipate or render the present invention obvious.

(Emphasis added.)

In response, the Examiner argued:

> The [Appellants] state that Chen et al. does not show the claimed step of deconvolving overlapping *data*. Chen et al. shows a method of resolving levels of two differently labeled fluorescent probes from the same location of an array after hybridization of two probes to the array. Chen et al. therefore deconvolves *data* consisting of the levels of two probes that physically overlap on the array. The claimed method is not interpreted to require more than that . . . .

(Emphasis added.)

Thus, the Examiner misinterprets the claims and takes the position that because Chen discloses the step of resolving overlapping data, it somehow anticipates the invention. However, the claims recite the step of "deconvolving overlapping portions of *distributions*." (Emphasis added.) Moreover, from the language of the claim, it will be appreciated that the distributions relate to the step of "deriving distributions of data obtained from physical measurements." A distribution of data is not the same thing as the data itself.

The McGraw-Hill Dictionary of Scientific and Technical Terms defines "distribution" in the statistical context (the present context) as:

> For a discrete random variable, a function (or table) which assigns to each possible value of the random variable the probability that this value will occur.

(McGraw-Hill Dictionary of Scientific and Technical Terms, S. P. Parker, Ed., 5th ed., page 596 (1994))

The fact that two particular measurements on different probes may overlap says absolutely nothing about the characteristics of their *distributions*. There is not the slightest suggestion in Chen that any derived data *distributions* might overlap, that deconvolving overlapping portions should be performed, or that it would be of any benefit. The fact that two samples might overlap has absolutely no significance in this regard.

Furthermore, referring to pages 369-370 of Chen, it is clear that all of the samples are assumed to have the same probability distribution. There is not the slightest suggestion that samples might be from two different distributions that overlap and need to be deconvolved.

In addition, convolution is not simply overlapping. Appellants have made of record a copy of an internet page (http://www.all-science-fair-projects.com/science_fair_projects_encyclopedia/Convolution) in which convolution is defined simply. Specifically, convolution is an operation which is performed between two *functions* and it produces a third *function*. This third function represents the overlap between the first function and the reverse, translated version of the second function. The definition provided notes that a convolution is a "kind of very general moving average." So, the invention deconvolves an effective moving average of an overlapping portion of two distributions.

Thus, knowing that two samples overlap tells us nothing about their probability distributions (functions), tells us nothing about whether the samples have overlapping probability distributions which are convolved, and certainly does not provide the slightest suggestion that the deconvolution operation be performed on the overlapping distributions of two variables to achieve anything of value.

The Appellants have requested that the Examiner specifically point out where in Chen there is the slightest suggestion of *distributions* needing to be deconvolved. However, he has never responded to this or even addressed the issue.

In the November 4, 2004 Advisory Action, the Examiner states that

> [t]he [Appellants] refer to a particular narrow definition of convolution. However it is not apparent from the specification that the term means anything other than the ordinary meaning of the term which is coiled or twisted with one part over another.

(Advisory Action, Item 5, continuation sheet.)

According to the McGraw-Hill Dictionary of Scientific and Technical Terms, the particular meaning of the term convolution relied on by the Examiner is in the context of anatomy.

> [ANAT] A fold, twist, or coil of any organ, especially any one of the prominent convex parts of the brain, separated from each other by depressions or suci.

(McGraw-Hill Dictionary of Scientific and Technical Terms, 6th ed., page 484 (2003).)

However, the definition of "convolution" in the mathematical and statistical context (the present context) as appearing in the McGraw-Hill Dictionary of Scientific and Technical Terms is as follows:

> [MATH] the convolution of the functions f and g is the function F, defined by
>
> $$F(x) = \int f(t)g(x-t)\,dt$$
>
> [STAT] A method for finding the distribution of the sum of two or more random variables; computed by direct integration or summation as contrasted with, for example, the method of characteristic functions.

(*Id.*)

Appellants submit that the dictionary definition of convolution within the mathematical and statistical contexts is in accord with the definition provided to the Examiner in the response to the final Office Action. Further, the definition of convolution relied on by the Examiner in

formulating his basis for not allowing the claims is not properly related to the subject matter recited in claims 5-7, 11, 14, 16 and 17. Because the Examiner raises for the first time the definition of convolution in his Advisory Action, for the convenience of the Board, Appellants have attached a photocopy of the dictionary definition in **Appendix B**.

It is respectfully submitted that, based upon the preceding discussion, the Examiner should be reversed.

VIII. EVIDENCE

All necessary evidence is in the record and discussed above, Namely, the dictionary definition of *distribution*, *deconvolution*, and *convolution*. However, it is believed that these are conventional definitions well known to those skilled in the art.

IX. RELATED PROCEEDINGS

There are no related proceedings for this matter.

X. CONCLUSION

For all of the reasons set forth above, the rejections of claim 5-7, 11, 14, 16, and 17 should be reversed. Appellants respectfully request that the application be remanded to the primary Examiner with an instruction to withdraw the 35 U.S.C. § 102(a) rejection, and pass the case to allowance.

Please charge any fee, except for the Issue Fee, that may be necessary for the continued pendency of this application to our Deposit Account No. 04-0100.

Dated: January 19, 2005

Respectfully submitted,

By _____
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APPENDIX A

Claims on Appeal for Application Serial No. 09/915,813

5. A method for discriminating among response classes of physical measurements obtained in hybridization arrays, comprising the steps deriving distributions of data obtained from the physical measurements and deconvolving overlapping portions of distributions.

6. The method of claim 5 wherein one of dual and multiple distributions derived from a measured array are modeled by mixture modeling.

7. The method of claim 5 wherein mixture modeling is used to determined the probability that any discrete array element falls within one of the modeled distributions.

11. The method of claim 7 used to evaluate physical measurements obtained from biological and chemical assays conducted in one of substrates, substrates containing wells, and test tubes.

14. The method of claim 6 wherein mixture modeling is used to determine the probability that any discrete array element falls within one of the modeled distributions.

16. The method of claim 5, used to evaluate physical measurements obtained from biological and chemical assays conducted on one of substrates, substrates containing wells, and test tubes.

17. The method of claim 6, used to evaluate physical measurements obtained from biological and chemical assays conducted on one of substrates, substrates containing wells, and test tubes.

McGRAW-HILL DICTIONARY OF SCIENTIFIC AND TECHNICAL TERMS

Sixth Edition

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On the cover: Representation of a fullerene molecule with a noble gas atom trapped inside. At the Permian-Triassic sedimentary boundary the noble gases helium and argon have been found trapped inside fullerenes. They exhibit isotope ratios quite similar to those found in meteorites, suggesting that a fireball meteorite or asteroid exploded when it hit the Earth, causing major changes in the environment. *(Image copyright © Dr. Luann Becker. Reproduced with permission.)*

Over the six editions of the Dictionary, material has been drawn from the following references: G. M. Garrity et al., *Taxonomic Outline of the Procaryotes*, Release 2, Springer-Verlag, January 2002; D. W. Linzey, *Vertebrate Biology*, McGraw-Hill, 2001; J. A. Pechenik, *Biology of the Invertebrates*, 4th ed., McGraw-Hill, 2000; *U.S. Air Force Glossary of Standardized Terms*, AF Manual 11-1, vol. 1, 1972; F. Casey, ed., *Compilation of Terms in Information Sciences Technology*, Federal Council for Science and Technology, 1970; *Communications-Electronics Terminology*, AF Manual 11-1, vol. 3, 1970; P. W. Thrush, comp. and ed., *A Dictionary of Mining, Mineral, and Related Terms*, Bureau of Mines, 1968; *A DOD Glossary of Mapping, Charting and Geodetic Terms*, Department of Defense, 1967; J. M. Gilliland, *Solar-Terrestrial Physics: A Glossary of Terms and Abbreviations*, Royal Aircraft Establishment Technical Report 67158, 1967; W. H. Allen, ed., *Dictionary of Technical Terms for Aerospace Use*, National Aeronautics and Space Administration, 1965; *Glossary of Stinfo Terminology*, Office of Aerospace Research, U.S. Air Force, 1963; *Naval Dictionary of Electronic, Technical, and Imperative Terms*, Bureau of Naval Personnel, 1962; R. E. Huschke, *Glossary of Meteorology*, American Meteorological Society, 1959; *ADP Glossary*, Department of the Navy, NAVSO P-3097; *Glossary of Air Traffic Control Terms*, Federal Aviation Agency; *A Glossary of Range Terminology, White Sands Missile Range, New Mexico*, National Bureau of Standards, AD 467-424; *Nuclear Terms: A Glossary*, 2d ed., Atomic Energy Commission.

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which only requires specifications about very few facts in order to be used by a programmer. [kən'vər·zhən rü'tēn]

conversion table [SCI TECH] A list of equivalent values for converting from one set of units to another. [kən'vər·zhən ˌtā·bəl]

conversion time [COMPUT SCI] The time required to read in data from one code into another code. [kən'vər·zhən ˌtīm]

conversive heating [MED] The conversion of some form of energy, especially radio waves, into heat for use in thermotherapy. [kən'vər·siv 'hēd·iŋ]

convert [COMPUT SCI] To transform the representation of data. [kən'vərt]

convertase [BIOCHEM] An enzyme that cleaves inactive protein precursors into smaller biologically active molecules. ['kän·vərˌtās]

converted water *See* product water. [kən'vərd·əd 'wȯd·ər]

converter [COMPUT SCI] A computer unit that changes numerical information from one form to another, as from decimal to binary or vice versa, from fixed-point to floating-point representation, from magnetic tape to disk storage, or from digital to analog signals and vice versa. Also known as data converter. [ELEC] 1. Any device for changing alternating current to direct current, or direct current to alternating current. 2. *See* synchronous converter. [ELECTR] 1. The section of a superheterodyne radio receiver that converts the desired incoming radio-frequency signal to the intermediate-frequency value; the converter section includes the oscillator and the mixer-first detector. Also known as heterodyne conversion transducer; oscillator-mixer-first detector. 2. An auxiliary unit used with a television or radio receiver to permit reception of channels or frequencies for which the receiver was not originally designed. 3. In facsimile, a device that changes the type of modulation delivered by the scanner. 4. Unit of a radar system in which the mixer of a superheterodyne receiver and usually two stages of intermediate-frequency amplification are located; performs a preamplifying operation. *See* remodulator. [MET] A type of furnace in which impurities are oxidized out by blowing air through or across a path of molten metal or matte. [NUCLEO] 1. Also known as nuclear converter. 2. A nuclear reactor that converts fertile atoms into fuel by neutron capture, using one kind of fuel and producing another. 3. A nuclear reactor that produces some fissionable fuel, but less than it consumes; the fuel produced may be the same as that consumed or different. [kən'vərd·ər]

converter substation [ELEC] An electric power substation whose main function is the conversion of power from ac to dc, and vice versa. [kən'vərd·ər 'səbˌstā·shən]

converter tube [ELECTR] An electron tube that combines the mixer and local-oscillator functions of a heterodyne conversion transducer. [kən'vərd·ərˌtüb]

convertiplane [AERO ENG] A hybrid form of heavier-than-air craft capable, because of one or more horizontal rotors or units acting as rotors, of taking off, hovering, and landing in a fashion similar to a helicopter; and once aloft and moving forward, capable, by means of a mechanical conversion, of flying purely as a fixed-wing aircraft, especially in higher speed ranges. [kən'vərd·əˌplān]

convex [SCI TECH] Having a curved form which bulges outward, resembling the exterior of a sphere or cylinder or a section of these bodies. ['känˌveks]

convex angle [MATH] A polyhedral angle that lies entirely on one side of each of its faces. ['känˌveks 'aŋ·gəl]

convex body [MATH] A convex set that has at least one interior point. ['känˌveks 'bäd·ē]

convex combination [MATH] A linear combination of vectors in which the sum of the coefficients is 1. ['känˌveks ˌkäm·bə'nā·shən]

convex curve [MATH] A plane curve for which any straight line that crosses the curve crosses it at just two points. ['känˌveks 'kərv]

convex function [MATH] A function $f(x)$ is considered to be convex over the interval a,b if for any three points x_1, x_2, x_3 such that $a < x_1 < x_2 < x_3 < b$, $f(x_2) \leq L(x_2)$, where $L(x)$ is the equation of the straight line passing through the points $[x_1, f(x_1)]$ and $[x_3, f(x_3)]$. ['känˌveks 'fəŋk·shən]

convex function in the sense of Jensen [MATH] A function $f(x)$ over an interval a, b such that, for any two points x_1 and x_2 satisfying $a < x_1 < x_2 < b$, $f[(x_1 + x_2)/2] \leq (1/2)\,(f(x_1) + f(x_2))$. ['känˌveks 'fəŋk·shən in thə ˌsens əv 'jen·səs]

convex hull [MATH] The smallest convex set containing a given collection of points in a real linear space. Also known as convex linear hull. ['känˌveks 'həl]

convex linear combination [MATH] A linear combination in which the scalars are nonnegative real numbers whose sum is 1. ['känˌveks ˌlin·ē·ər ˌkäm·bə'nā·shən]

convex linear hull *See* convex hull. ['känˌveks ˌlin·ē·ər ˌhəl]

convexo-concave [SCI TECH] Having one side convex and the other concave, usually with greater curvature on the convex side. Also known as concavo-convex. [kənˌvek·sō'kän]

convex polygon [MATH] A polygon all of whose interior angles are less than or equal to 180°. ['känˌveks 'päl·iˌgän]

convex polyhedron [MATH] A polyhedron in the plane which is a convex set, for example any regular polyhedron. ['känˌveks ˌpäl·i'hē·drən]

convex polytope [MATH] A bounded, convex subset of an n-dimensional space enclosed by a finite number of hyperplanes. ['känˌveks 'päl·iˌtōp]

convex programming [MATH] Nonlinear programming in which both the function to be maximized or minimized and the constraints are appropriately chosen convex or concave functions of the independent variables. ['känˌveks 'prōˌgram·iŋ]

convex sequence [MATH] A sequence of numbers, $a_1, a_2, \ldots$, such that $a_{i+1} \geq (1/2)(a_i + a_{i+2})$ for all $i \geq 1$ (or for all i satisfying $1 \leq i < n - 2$ if the sequence is a finite sequence with n terms). ['känˌveks 'sē·kwəns]

convex set [MATH] A set which contains the entire line segment joining any pair of its points. ['känˌveks 'set]

convex span [MATH] For a set A, the intersection of all convex sets that contain A. ['känˌveks 'span]

conveyor [MECH ENG] Any materials-handling machine designed to move individual articles such as solids or free-flowing bulk materials over a horizontal, inclined, declined, or vertical path of travel with continuous motion. [kən'vā·ər]

conveyor belt balance [ENG] A balance used for weighing unpackaged, loose, continuously transported material on a conveyor belt by weighing the load being moved and measuring the belt speed. [kən'vā·ər ˌbelt ˌba·ləns]

convivium [ECOL] A population exhibiting differentiation within the species and isolated geographically, generally a subspecies or ecotype. [kən'viv·ē·əm]

convolute [BIOL] Twisted or rolled together, specifically referring to leaves, mollusk shells, and renal tubules. ['kän·vəˌlüt]

convolute bedding [GEOL] The extremely contorted laminae usually confined to a single layer of sediment, resulting from subaqueous slumping. ['kän·vəˌlüt ˌbed·iŋ]

convolution [ANAT] A fold, twist, or coil of any organ, especially any one of the prominent convex parts of the brain, separated from each other by depressions or sulci. [GEOL] 1. The process of developing convolute bedding. 2. A structure resulting from a convolution process, such as a small-scale but intricate fold. [MATH] The convolution of the functions f and g is the function F defined by

$$F(x) = \int_0^x f(t)g(x - t)\,dt$$

[STAT] A method for finding the distribution of the sum of two or more random variables; computed by direct integration or summation as contrasted with, for example, the method of characteristic functions. [ˌkän·və'lü·shən]

convolutional code [COMMUN] An error-correcting code that processes incoming bits serially rather than in large blocks. [ˌkän·vəlü·shən·əl 'kōd]

convolution family *See* faltung. [ˌkän·və'lü·shən ˌfam·lē]

convolution rule [MATH] The statement that $C(p + q, r)$ is the sum over the index j from $j = 0$ to $j = r$ of the quantity $C(p, j)\,C(q, r - j)$, where, in general, $C(n, r)$ is the number of distinct subsets of r elements in a set of n elements (the binomial coefficient). Also known as Vandermonde's identity. [ˌkän·və'lü·shən ˌrül]

convolution theorem [MATH] A theorem stating that, under

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Atty Docket No.: 01191/100E235-US2

Inventor: Peter Ramm et al.

Appln: 09/915,813-Conf. Filed: Jul. 25, 2001

Title: PROCESS FOR EVALUATING CHEMICAL AND BIOLOGICAL ASSAYS

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